PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference TYDS:205370551	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. **PCT/AU2004/001032**	International filing date *(day/month/year)* 4 August 2004	Priority date *(day/month/year)* 6 August 2003
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] G01N 27/447, 27/453, B01D 57/02		
Applicant GRADIPORE LIMITED et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
25 February 2005	30 June 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **JULIA HU** Telephone No. (02) 6283 2754

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001032

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **2-8, 10-15** as originally filed/furnished
pages* **1, 9** received by this Authority on **25 February 2005** with the letter of **25 February 2005**
pages* received by this Authority on with the letter of

☒ the claims:

pages **19** as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **16-18** received by this Authority on **25 February 2005** with the letter of **25 February 2005**
pages* received by this Authority on with the letter of

☒ the drawings:

pages **1/10-10/10** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-21	YES
	Claims		NO
Inventive step (IS)	Claims	1-21	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-21	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

NOVELTY (N) AND INVENTIVE STEP (IS) claims 1-21

The invention of the claims is an electrophoresis membrane support with all of the features defined in the main claim 1, which in use can change flow configuration to direct and control a large volume transverse flow.

All the documents cited in the International Search Report were category A only. No individual citation or obvious combination of citations disclose or fairly suggest such a membrane support which supports a membrane and provides flow of fluid over the membrane in a controlled and efficient manner. Therefore, the claimed invention is considered to be novel and inventive.

ELECTROPHORESIS MEMBRANE SUPPORT AND MANIFOLD UNIT

Technical Field

The present invention relates to a membrane support and manifold adapted to accept one or more membranes suitable for use in an electrophoresis apparatus.

Background Art

Membrane-based electrophoresis is a new technology originally developed for the separation of macromolecules such as proteins, nucleotides and complex sugars. This unique preparative electrophoresis technology originally developed for macromolecule separation utilises tangential flow across polyacrylamide membranes with an electric field or potential applied across the membranes. The general design of the system facilitates the purification of proteins and other macromolecules under near native conditions. This results in higher yields and excellent purity. The process provides a high purity, scalable separation that is faster, cheaper and higher yielding than current methods of macromolecule separation. Furthermore, the technology offers the potential to concurrently purify and decontaminate macromolecule solutions.

To scale up any separation technology for commercial applications, new apparatus design and technology are often required. To scale up membrane-based electrophoresis based on the original Gradiflow™ technology developed by Gradipore Limited (see US 6413402; US 6328869; US 5039386; US 5650055 and WO 02/24314), the present inventors found it was necessary to significantly alter many of the components of the apparatus to accommodate large membranes and overcome problems encountered with scale-up.

The present inventors have developed an improved membrane support and manifold for use in larger scale membrane-based electrophoresis.

Disclosure of Invention

In a first aspect, the present invention provides an electrophoresis membrane support comprising:

a substantially planar member having four boundaries, an upper face and a lower face;

an inlet port disposed near one boundary;

an outlet port disposed opposite the inlet port near an opposite boundary;

(cathode). Conversely, a negatively-charged ion will move toward the positive electrode (anode).

Membrane-based electrophoresis apparatus (Gradiflow™) developed by, or in association with, Gradipore Limited, Australia are suitable for performing the methods described herein and are fully disclosed in commonly assigned US 6413402, US 6328869, US 5039386, US 5650055 and WO 02/24314. The apparatus may include a cartridge which houses a number of membranes forming at least two chambers, a cathode and an anode in respective electrode chambers connected to a suitable power supply, reservoirs for samples, buffers and electrolytes, pumps for passing samples, buffers and electrolytes, and cooling means to maintain samples, buffers and electrolytes at a required temperature during electrophoresis. The cartridge typically contains at least three substantially planar membranes disposed and spaced relative to each other to form two chambers through which sample or solvent can be passed. A separation membrane is disposed between two outer membranes (termed restriction membranes as their molecular mass cut-offs are usually smaller than the cut-off of the separation membrane). When the cartridge is installed in the apparatus, the restriction membranes are typically located adjacent to an electrode. One example of a cartridge is described in AU 738361.

In the apparatus, ion-permeable barriers that substantially prevent convective mixing between the adjacent chambers of the manifold according to the present invention are placed in an electric field and components of the sample are selectively transported through the ion-permeable barriers. The particular ion-permeable barriers used will vary for different applications and generally have characteristic average pore sizes and pore size distributions and/or isoelectric points allowing or substantially preventing passage of different components.

Having outlined some of the principles of operation of an apparatus, a manifold and separation unit will be described.

Figure 1 shows a preferred concept of the present invention providing transverse flow of fluid in adjacent chambers formed by three membranes. The change in flow configuration, although difficult to develop and engineer, results in significant improvement in electrophoresis separation. A transverse flow allows more efficient flow of material over the membranes, reduced void volumes, less gas build-up, and increased separation efficiency. A new membrane support to direct and control liquid flow had to be developed that would allow this new configuration of the electrophoresis separation unit. It will be appreciated, however, that the membrane support can be used alone in an

Claims:

1. An electrophoresis membrane support comprising:

a substantially planar member having four boundaries, an upper face and a lower face;

an inlet port disposed near one boundary;

an outlet port disposed opposite the inlet port near an opposite boundary;

spacers positioned between the inlet port and outlet port adapted to support a membrane positioned on the upper face or on the lower face of the member;

interstitial space disposed between the spacers capable of allowing flow of fluid therein;

inlet means in fluid communication with the inlet port and the interstitial space;

outlet means in fluid communication with the interstitial space and the inlet port, the inlet and outlet means adapted to allow flow of fluid along the interstitial space;

first flow port disposed near one boundary; and

second flow port disposed opposite the first flow port near an opposite boundary, the first and second flow ports direct flow of fluid to or from the electrophoresis apparatus.

2. The support according to claim 1 wherein two supports are adapted to be assembled in an electrophoresis apparatus or cartridge to form transverse fluid flow paths along respective interstitial spaces formed by each support.

3. The support according to claim 1 or 2 wherein at least some of the inlet, outlet and flow ports are provided as channels formed in each respective boundary of the member.

4. The support according to claim 1 or 2 wherein at least some of the inlet, outlet and flow ports are formed as a plurality of ports or holes in the member.

5. The support according to claim 1 or 2 wherein the inlet and outlet ports are formed as non-circular ports to assist in movement of fluid in the port to enter the inlet or outlet means.

6. The support according to any one of claims 1 to 5 wherein the spacers are formed as a plurality of substantially planar parallel members running from the inlet means to the outlet means.

7. The support according to any one of claims 1 to 6 wherein the inlet means is formed by a series of flow channels directing fluid from the inlet port to the interstitial space.

8. The support according to any one of claims 1 to 7 wherein the outlet means is formed by a series of flow channels directing fluid from the interstitial space to the outlet port.

9. The support according to any one of claims 1 to 8 being substantially square in shape with the ports disposed near each of the four boundaries forming the square.

10. The support according to any one of claims 1 to 9 further comprising one or more drain ports.

11. The support according to claim 10 wherein the drain ports are in communication with drain channels adapted to receive fluid escaped from the ports or interstitial spaces.

12. An electrophoresis separation unit comprising:

a first manifold having at least one inlet port and one outlet port;

a second manifold having at least one inlet port and one outlet port;

a plurality of electrophoresis membrane supports according to any one of claims 1 to 11 disposed between the first manifold and the second manifold; and

a plurality of ion-permeable membranes disposed between the membrane supports forming a plurality of adjacent flow chambers between the membranes;

wherein in use the direction of flow of fluid in one flow chamber is transverse to the direction of flow of another flow chamber.

13. The separation unit according to claim 12 having two membrane supports and three membranes forming a first flow chamber and a second flow chamber.

14. The separation unit according to claim 13 wherein the first manifold includes a first inlet port and first outlet port in fluid communication with the first chamber and a second inlet port and second outlet port in communication with the second chamber.

15. The separation unit according to claim 13 wherein the second manifold includes a first inlet port and first outlet port in communication with the first chamber and a second inlet port and second outlet port in communication with the second chamber.

16. The separation unit according to any one of claims 12 to 15 further containing an electrode associated with both the first and second manifolds.

17. The separation unit according to claim 12 comprising:

a first manifold having a first inlet port and first outlet port, a second inlet port and second outlet port, and a third inlet port and a third outlet port;

a second manifold having an inlet port and outlet port;

a first ion-permeable membrane disposed adjacent the first manifold;

a second ion-permeable membrane disposed adjacent the first ion-permeable membrane;

a third ion-permeable membrane disposed adjacent the second manifold;

a first membrane support disposed between the first ion-permeable membrane and the second ion-permeable membrane;

a second membrane support disposed between the third ion-permeable membrane and the second ion-permeable membrane;

a first fluid chamber adapted to receive fluid in a first stream disposed between the first ion-permeable membrane and the second ion-permeable membrane;

a second fluid chamber adapted to receive fluid in a second stream between the second ion-permeable membrane and the third ion-permeable membrane;

a first electrolyte chamber containing a first electrode disposed between the first ion-permeable membrane and the first manifold; and

a second electrolyte chamber containing a second electrode disposed between the third ion permeable membrane and the second manifold;

wherein the first inlet port and first outlet port are in fluid communication with the first fluid chamber, the second inlet port and second outlet port are in fluid communication with the second fluid chamber, the third inlet port and third outlet port are in fluid communication with the first electrolyte chamber, and the inlet port and outlet port are in fluid communication with the second electrolyte chamber, and

wherein in use the direction of flow of the first steam is transverse to the direction of flow of the second stream.

18. The separation unit according to any one of claims 12 to 17 wherein at least one ion permeable membrane is a hydrogel membrane, an endo-electro-osmosis membranes capable of controlling the bulk movement of water, an isoelectric membrane, or a membrane having defined pore size or pore size distribution.